REMARKS

Applicant has carefully considered the positions of the Examiner, and respectfully requests reconsideration based upon the manifest differences between the present invention and the cited references. In the October 30, 2003, Office Action the Examiner rejected claims 1-14 under 35 U.S.C. §§ 112, 102 and/or 103. Applicant herein responds to those rejections and highlights the differences between the pending claims and the cited references such that it becomes apparent to the Examiner that these rejections should be reconsidered and withdrawn. Applicant respectfully submits the Examiner's reliance upon the prior art is misplaced as applicant's invention is very different from what is disclosed in these references. In particular, applicant would like to direct the Examiner's attention to applicant's novel system method for analyzing a complex biological sample, which allows for the ability to conduct drug testing analysis in minutes, rather than weeks or months. Moreover, applicant has amended the claims to more clearly define the unique and non-obvious features of the present invention.

With respect to the §112 rejections, applicant has amended the claims in accordance with the Examiner's comments. Applicant thanks the Examiner for calling these issues to his attention.

Initially, the Examiner rejected claims 1-2 and 4-10 under 35 U.S.C. § 102(b) as being anticipated by Yates, *J. Mass Spectrom.*, Vol. 33, 1-19, 1998, ("Yates"). Applicant respectfully submits that the Examiner's reliance on Yates is misplaced. It is black letter law that to be anticipatory, a prior art reference must disclose each and every element of the claim or claims at issue -- Yates falls far short of this requirement.

Briefly, Yates discusses the use of mass spectrometry as a tool to correlate proteins to their respective genes. According to Yates, this technique has become possible through improvements in mass analysis techniques and the large-scale sequencing of DNA for entire genomes. Yates merely provides a tutorial on principles of ionization and mass analysis for peptides and proteins. Specifially, Yates describes methods utilizing matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI) for identifying and sequencing proteins. In his tutorial, Yates also discusses database searching methods to identify amino acid sequences represented in a mass spectrum, and thereby identify the protein. This is very different from the present invention.

Specifically, as claimed, the present invention relates to a method for analyzing complex biological samples, such as drug-dosed cellular samples, using a Fourier Transform Mass Spectrometer, comprising the steps of ionizing the drug-dosed sample to produce sample ions, introducing said sample ions into an analysis region of said Fourier Transform Mass Spectrometer, analyzing said sample ions to determine the molecular weight and abundance of said sample ions, utilizing said molecular weight to determine the empirical formula of each species of said sample, and identifying each of said species by comparing said empirical formula to a database of formulas for known molecules. This is very different from the process described by Yates for ----- reasons. First, nowhere does Yates discuss the use of mass spectrometry as a tool to study the interaction between small and large molecules. Yates merely discusses the analysis of a pure sample of a singe peptide or protein, or at most a protein complex. In contrast, the present invention is capable of analyzing more complex systems where it is not necessary to prepare a purified sample for analysis in the mass spectrometer. Second, Yates does not discuss a method that allows for the ability to observe all effects

of a drug on test cells, as does the present invention. This monitoring and characterization of all detectable chemical changes in a cell following drug-dosage has never before been accomplished. Third, the present invention allows a researcher to maintain throughput by observing cellular reactions (involving several compounds), adjusting parameters accordingly, viewing the results, and then continuing with experimentation. This throughput would not be maintained with the methods described by Yates, as Yates only analyzes purified samples. Consequently, in view of the foregoing, the applicant respectfully requests that this rejection be reconsidered and withdrawn – at least one element of the claimed invention in Claims 1-2 and 4-10 is not taught or disclosed by Yates.

Next, under 35 U.S.C. § 103(a), the Examiner rejected Claims 3 and 11 as being unpatentable over Yates (as applied to claims 1 and 9) in view of Moore et al. U.S. Patent No. 5,577,239 ("Moore"), rejected claims 12 and 13 as being unpatentable over Yates in view of Franzen et al. U.S. Patent No. 5,663,561 ("Franzen"), and rejected claim 14 as being unpatentable over Yates and Franzen in view of Moore. Applicant respectfully disagrees and submits that the Examiner's application of the teachings of the cited references is misplaced. More particularly, applicant disagrees with the Examiner's opinion as to the specific teachings of the cited references, any resulting combination thereof, and the application of these teachings to the claimed invention.

With regard to the rejection of Claims 3 and 11-14, as discussed above, Yates fails to teach a method for monitoring and characterizing all detectable chemical changes in a cell following drug-dosage. Rather, Yates merely teaches using mass spectrometry to identify a single, purified sample of a specific protein. Similarly, neither Moore nor Franzen teach the use of mass spectrometry to determine empirical formulas or molecular structures. In short, Moore merely discloses a storage, searching and

retrieval system for chemical structures, and Franzen merely teaches a method of ionizing non-polar samples.

Consequently, none of the references relied on by the Examiner teach or suggest each and every element of the claimed invention of the pending claims. In fact, none of the cited references teach or suggest a method for analyzing complex biological samples that have been drug-dosed, utilizing Fourier Transform Mass Spectrometry, which allows a researcher to constantly and immediately monitor the effects of a drug on test cells. Therefore, applicant submits that the rejection of claims 3 and 11-14 as being unpatentable over Yates, Moore and/or Franzen should be reconsidered and withdrawn.

Furthermore, despite the fact that a combination of the cited references does not teach the claimed invention, applicant submits that such a combination is improper as merely an "obvious to try" argument. In fact, each of the methods disclosed in Yates, Moore and Franzen are inadequate for the determination of immediate effects of a drug on test cells. Furthermore, nowhere do the cited references address the analysis of complex biological samples which have been injected with drugs, nor do they address the ability to test and identify all changes in cellular composition through the use of FTMS, as does the present invention. Accordingly, it cannot be said that the present invention is obvious in view of Yates, Moore and/or Franzen alone or in combination. At best it might be "obvious to try" such a combination, which, is not the standard for obviousness under 35 U.S.C. §103. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 91 (Fed. Cir. 1986).

Under the circumstances, applicant re-submits that the Examiner has succumbed to the "strong temptation to rely on hindsight." *Orthopedic Equipment Co. v. United States*, 702 F.2d 1005, 1012,

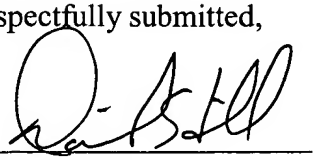
217 U.S.P.Q. 193, 199 (Fed. Cir. 1983). The only "motivation" for the Examiner's combination of the cited references is provided by the teachings of applicant's own disclosure. No such motivation is provided by the references themselves. The present invention monitors and characterizes all detectable chemical changes in a cell following drug dosage. In contrast, Yates teaches determining the structure of a single protein, Moore teaches a chemical database for known molecules, not for experimental results, and Franzen merely teaches an ionization method. None of the cited references, either alone or in combination, teaches the unique and non-obvious features of the present invention. Therefore, as is evidenced by the above amendments and remarks, the present invention, for the first time, discloses a method for the analysis of complex biological samples utilizing FTMS which allows for the constant and immediate monitoring of the effects of a drug on the sample.

CONCLUSION

In view of the foregoing, applicant respectfully submits that the present invention represents a patentable contribution to the art and the application is in condition for allowance. Early and favorable action is accordingly solicited.

Date: April 30, 2004

Respectfully submitted,



David M. Hill
Reg. No. 46,170
WARD & OLIVO
708 Third Avenue
New York, New York 10017
(212) 697-6262